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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 20

Application Number: 09/139,058
Filing Date: August 24, 1998
Appellant(s): Woodle et al

Judy M Mohr
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 12-28-00.

(1) ***Real Party in Interest***

A statement identifying the real party in interest is contained in the brief.

(2) ***Related Appeals and Interferences***

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Claims 8-9 and 11-19 stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

4,897,384	**Janoff et al**	**1-1990**
4,981,692	**Popescu et al**	**1-1991**
5,593,622	**Yoshioka et al**	**1-1997**

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 U.S.C. § 103

1. Claims 8-9 and 11-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janoff ((4,897,384) or Popescu (4,981,692) in view of Yoshioka (5,593,622).

Janoff teaches gentamicin containing liposomes (note the abstract, examples and claims). Janoff however, does not teach that the phospholipids used in the formation of liposomes be attached with the hydrophilic polymer such as polyethylene glycol (PEG).

As pointed out above, Popescu teaches liposome formulations containing gentamicin. Popescu although teaches that cholesterol-PEG could be used in the liposomes, does not teach that phospholipids used in the formation of liposomes be attached with the hydrophilic polymer, polyethylene glycol (PEG).

Yoshioka teaches that when phospholipids which are attached to PEG are used in the formation of liposomes, the hydrophilic moiety of PEG prevents the adsorption of plasma proteins on the liposomes and the subsequent agglutination of liposomes (note the

abstract). In essence Yoshioka indirectly teaches that the stability of the liposomes is increased.

The attachment of PEG to the surface of the liposomes (by coupling with the phospholipid) taught by Janoff or Popescu would have been obvious to one of ordinary skill in the art because PEG prevents the adsorption of plasma proteins on the liposomes and the subsequent agglutination of liposomes as taught by Yoshioka.

Applicants' arguments have been fully considered, but are not found to be persuasive. Applicants argue that Janoff lists four embodiments (applicants omit Janoff's teachings of liposomes using various phospholipids, as evident from col. 8, line 58 through line 17) and that the important feature of the Janoff preparation appears to be the ability of the selected ligand to competitively bind with the toxicity receptor and that the modification of the phospholipid head group with a PEG chain will prevent such a binding. This argument is not found to be persuasive for the following reason. If that were to be the rationale, amphotericin B which is complexed with PEG-cholesterol, also taught by Janoff (but not as a liposomal preparation, as correctly pointed out by applicants) would not have been effective against inhibiting the growth of C. albicans studied by Janoff since PEG would not have bound to the toxicity receptor. The very fact that Janoff finds that amphotericin - PEG cholesterol complex is effective against the organism shows that PEG has a positive effect in binding to the toxicity receptor (see Tables V and VI on columns 17 and 18). This actually strengthens the examiner's position that one skilled in the art would

be motivated to use PEG since the secondary reference of Yoshioka teaches an additional motivation for one skilled in the art to use PEG in the liposomes. Furthermore, if applicant's reasoning that modification of the liposomal surface by attachment with PEG would prevent the binding of the drug and thus defeating the purpose for which it is used for in the prior art, then the examiner points out that Janoff would not have suggested the use of PEG at all. The examiner also points out that cholesterol being lipophilic, just like other amphiphilic lipids, it would be associated with the membrane of the liposomes and PEG in PEG-cholesterol taught by Janoff would naturally be exposed on the surface of the liposomes. Therefore, one skilled in the art would be motivated to attach PEG to an amphiphilic lipid since the secondary reference clearly teaches that PEG increases the stability of the liposomes. The examiner also points out the motivation for one to use PEG need not be the same as applicant's.

Applicants' argue that Popescu is concerned with RES and that Popescu teaches away since as well known in the art that liposomes containing polymer -derivatized lipid avoid uptake by the RES. These arguments are not found to be persuasive. As pointed out in the final rejection, on columns 4 and 5 Popescu only refers to the sites the bacteria is likely to infect (cells of the reticuloendothelial system). On column 5, line 42 et seq.,

Popescu clearly teaches that his invention is not limited to the treatment of intracellular infections, but can be "*directed to a variety of sites of infection whether intracellular or extracellular*". The examiner also points out that it is common knowledge that bacteria can attack a variety of tissues which are not in the reticuloendothelial system (RES). Besides what is taught by Popescu is direct intra mammary infusion which does not involve RES (note col. 1, lines 14-20). Furthermore, as pointed out before, Popescu also advocates on col. 4, lines 7-8 the use of PEG-cholesterol which substantiates that Popescu's compositions are meant to treat infections irrespective of the site of infection. Therefore, one skilled in the art would use PEG since according to the secondary reference, it increases the stability of the liposomes. As pointed out above, the motivation to use PEG need not be the same as applicants'.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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March 29, 2001

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